REMARKS/ARGUMENTS

Claims 1-47 were cancelled.

Claim 48 is currently amended.

Claim 49 is currently amended.

Claim 54 was cancelled.

Claim 55 is cancelled.

Claim 61 is currently amended.

Claim 62 is currently amended.

Claims 50-53, 56-60, 63-74 are unchanged from the immediate prior version.

The amendment of claims 48 and 61 is related to the permeabilizing agent: according to the invention, the function of the permeabilizing agent is to create a hydrophilic network, thus assisting the fast-disintegration of the tablet and moreover, allowing to reduce the amount of lubricants needed to ensure optimum manufacturing conditions, and to reduce the intensity of the compression needed to produce a tablet.

CLAIM REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH

In Claim 48, the term "said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid" was already deleted (see amendment filed July 21, 2003).

CLAIM REJECTIONS UNDER 35 USC § 112, SECOND PARAGRAPH

In Claim 49, the term "lubricants" is deleted. Claim 49 is amended to make clear that the mixture of excipients further comprises at least one from the group consisting of sweeteners, flavorings and colors.

Claim 62 is amended accordingly.

CLAIM REJECTIONS UNDER 35 USC § 103 (a) as being unpatentable over Liu et al. (US 6,465,009) in view of Ku et al. (US 5,994,348)

Liu et al. teach a rapidly disintegrated tablet containing an active ingredient and an excipient comprising a disintegration agent, a polyol and a lubricant.

Regarding the **polyol**, Liu et al. disclose the use of mannitol as filler, but they do not describe the use of directly compressible mannitol.

The **disintegration agent** used in Liu's example is PVP. PVP is mentioned in Liu et al. as the essential disintegration agent (see e.g. col.14, l.44-47, see also claim 1). The term "PVP" relates to a **water-soluble** polymer (see e.g. col.6, l.41). Liu et al. insist on the fact that a water-soluble polymer is an essential feature (see e.g. col.6 l.29-30 and claim 1).

Liu et al. cite the possible use of croscarmellose, as an agent that can be added in the formulation already containing PVP. But Liu and al. do not mention that croscarmellose could be used alone in a composition, as sole disintegration agent.

The use of croscarmellose is not presented in Liu et al. examples.

The amount of croscarmellose that could be added in the tablet is not disclosed either.

This means that Liu et al disclose an excipient having a disintegration agent being water-soluble PVP, optionally added with croscarmellose, a polyol, and a lubricant.

As acknowledged by the Examiner, the inclusion of a permeabilizing agent is not taught by Liu et al.

There is no incentive for one skilled in the art, willing to make a rapidly disintegrating tablet, to turn to Ku et al., since Ku et al relate to a small, easily swallowed tablet, not intended to stay in the oral cavity for disintegration.

Ku et al. teach the use of croscarmellose as sole disintegration agent, in combination with a diluent, a binder, a lubricant and SiO_2.

SiO_2 is not known as a permeabilizing agent, but as providing "a superior lubrication effect as minimizing any decline in tablet dissolution performance (see col.5 l.59-92)".

It is the Examiner's view that one skilled in the art knowing Liu et al. and Ku et al. would have combined the two teachings. The Applicant respectfully disagrees for the reasons formerly presented.

It is also the Examiner's view that Liu et al. is the closest prior art, and that one skilled in the art would start from Liu et al. teaching, and combine it with Ku et al. teaching regarding the lubricant enhancer.

If so, one skilled in the art might have obtained a formulation where the disintegration agent is PVP (a water soluble polymer), optionally combined with croscarmellose, a polyol, a lubricant, and SiO2.

This formulation differs from the instant invention :

1) the instant invention teaches that the disintegration agent is selected from the group consisting of **croscarmellose, crospovidone**, and mixture thereof.

Crospovidone is a **water-insoluble** polymer : using a water-insoluble polymer is not considered in Liu et al. On the contrary, it is recommended to use water-soluble polymer.

Croscarmellose is also a **water-insoluble** polymer.

Thus, the instant invention is directed to the use of one water-insoluble polymer alone, or of the mixture of two water-insoluble polymers.

This is not taught nor suggested by Liu et al. The teaching of Ku et al. relating to croscarmellose only would not be taken into consideration by one skilled in the art, since Ku et al. do not concern tablets to be disintegrated in the oral cavity.

2) The instant invention teaches that the polyol is under a specific form, i.e. it is directly compressible. This has high consequences on the formation of the tablet. This feature is not taught nor suggested by Liu et al, nor by Ku and al.

Thus, the combination of these two prior art, assuming that there would be an incentive to combine them, which is hereby contested, does not lead to the multiparticulate tablet of the instant invention, where the disintegration agent is selected from the group consisting of croscarmellose crospovidone and mixtures thereof, and where the polyol is directly compressible.

CLAIM REJECTIONS UNDER 35 USC § 103 (a) as being unpatentable over Augello et al.(US 6,099,865) in view of Myers et al. (US 5,567,439)

Augello et al. teach a method for masking the bitter taste of pharmaceuticals by coating particles of the active principle with croscarmellose. A binder, such as ethylcellulose or PVP can be added to the croscarmellose. Sweeteners and granular mannitol can also be added.

The Applicant submits that Augello et al. does not relate to the manufacturing of a tablet from particles of coated active principle : Augello et al. relate to the **coating** of active principle particles.

Thus, the starting component is, in Augello et al., different from the starting component of the invention.

Augello et al. indicate that croscarmellose is useful to mask the bitter taste of bitter active principles, and has to be used in an amount of 10-50 %, preferably 15-28%, more preferably 18-25 % (see col.2 line 58-65).

Reading Augello et al., one skilled in the art is not directed to use croscarmellose on already-coated particles, but to use croscarmellose as a coating (see e.g. table 3 col.7). Moreover, one skilled in the art is not incented to use croscarmellose in the range of 1-15 %, as Augello et al. teach higher ranges.

As acknowledged by the Examiner, Augello et al. do not recite a permeabilizing agent.

Thus, the instant claimed invention differs from Augello et al. in that the instant invention relates to a **tablet** based on particles of **coated** active principle and in containing a permeabilizing agent, where Augello et al. relate to a composition based on active principle powder.

Myers et al. teach a delivery of controlled-release system, which is a sugar unit, containing sugars, flavours, sweeteners and glidants. Myers et al. differ from the instant invention in that Myers et al. do not recite croscarmellose or crospovidone as possible disintegration agent, and do not indicate a 1-15 % range amount of disintegration agent in the tablet.

Moreover, Myers et al. recite a long list of possible sugars, where the instant invention selects a directly compressible polyol having less than 13 carbon atoms, with an average particle diameter of 100 to 500 microns.

Therefore, one skilled in the art knowing Augello et al. could not deduce that it was of interest to treat again an already coated active principle powder with a further process using croscarmellose.

The information found by one skilled in the art in Myers et al. could have lead him to use glidants, but only in order to make a first coating on active principle powder.

There is neither teaching nor suggestion in Augello et al regarding a further treatment of an already-coated active principle powder.

Moreover, Augello et al. do not teach that selecting a specific polyol, as in the instant invention, could be of interest. This selection is neither described nor suggested in Myers et al. either.

Therefore, Augello et al., in view of Myers et al., do not lead to the claimed invention.

NON STATUTORY DOUBLE PATENTING REJECTION

It is respectfully submitted that, in the instant application, a permeabilizing agent is needed and is an essential feature of the tablet, as set forth in amended claim 48 above. The Applicant precises the nature of the permeabilizing agent by amending claim 48, in order to make clear that the required permeabilizing agents are selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

The permeabilizing agent of the instant invention is of particular importance, since it favors the rearrangements of particles during compression and allows using a reduced intensity of compression, leading to a tablet with improved palatability.

This feature does not exist in claim 1 of US 6,106,861 and one skilled in the art could not deduce from any claim of US 6,106,861 that this ingredient was of particular importance.

Hence, the instant application includes a technical feature which was not claimed in US 6,106,861 and was not obvious from this patent either.

It is respectfully submitted that the presence of this new technical feature makes the instant patent application a patentably distinct invention from US 6,106,861.

Consequently, Applicants allege the rejection of claims 48-74 under 35 USC should be withdrawn, as well as the double patenting objection.

In view of the above remarks, Applicant respectfully requests that a timely Notice of Allowance be issued in this case. If there are any remaining issues which can be expedited by a telephone conference, the examiner is courteously invited to telephone the counsel at the number indicated below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

September 22, 2004

By _____
Kevin A. Keeling
Registration No. 51,867
Customer No. 03000
(215) 567-2010
Attorneys for Applicants

Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.